PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:	Docket No: **Q101074**
Takashi HORIGUCHI et al.	Conf. No.: **9679**
Appln. No.: **10/547,843**	Group Art Unit: **1649**
Filed: **September 6, 2005**	Examiner: **Chernyshev, Olga**

For: **NOVEL PROTEIN AND ITS DNA**

REPLY BRIEF PURSUANT TO 37 C.F.R. § 41.41

MAIL STOP APPEAL BRIEF - PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In accordance with the provisions of 37 C.F.R. § 41.41, Appellants respectfully submit this Reply Brief in response to the Examiner's Answer dated October 2, 2009. Entry of this Reply Brief is respectfully requested.

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I. STATUS OF CLAIMS

Claims 1, 2, 4-7 and 17 are pending in the application. Claims 3, 8-16 and 18-36 are cancelled. All claims are currently rejected. This reply is directed to rejected claims 1, 2, 4-7 and 17.

II. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The grounds of rejection to be reviewed on appeal are whether the Examiner erred in rejecting claims 1, 2, 4-7 and 17 under 35 U.S.C. § 101 as allegedly lacking utility; 35 U.S.C. § 112, first paragraph as allegedly lacking enablement; and claim 17 under 35 U.S.C. § 112, second paragraph as allegedly being indefinite.[1]

[1] The rejections under 35 U.S.C. § 112 are contingent on the rejection under 35 U.S.C. § 101.

III. ARGUMENTS

The Examiner, and Conferees Stucker and Nickol, erred in rejecting claims 1, 2, 4-7 and 17 under 35 U.S.C. § 101 and 35 U.S.C. § 112, first and second paragraph for at least the following reasons.

A. Appellants' Claimed Proteins And Nucleic Acids Have A Function And Biological Significance

The Examiner's Answer alleges that Appellants' claimed proteins (e.g., C1) and the encoding nucleic acids lack utility because there is allegedly no disclosed function or biological significance of record. See, *inter alia*, pages 3, 4, 6 and 8, Examiner's Answer.[2]

Appellants respectfully disagree. The function and biological significance of Appellants' C1 polypeptide is however, clear from the record. As indicated at pages 13-19 of Appellants' Appeal Brief, the record shows the nexus between C1 (i.e., SEQ ID NO: 1) and enhanced expression in nerve cells subjected to endoplasmic reticulum (ER) stress. In other words, under ER stress C1 protein expression is significantly increased thereby indicating a direct role for C1 in the ER stress response. This alone is one function and biological significance of C1. Appellants have also proven that the expression of C1 is enhanced in rat primary nerve cells that

[2] Specifically, according to the Office, "The specification fails to disclose a specific biological function, relevance to a pathological condition, or any other basis for patentability, of the instant claimed molecules"; "the instant claims are drawn to an isolated nucleic acid molecule and the protein encoded thereby of as yet undetermined function or biological significance..."; "...a protein for which no biological function is known"; "the instant specification does not teach a biological activity of the protein..."; "the instant claims are drawn to an isolted nucleic acid molecule and the protein encoded thereby of as yet undetermined function or biological properties". See, *inter alia*, pages 3, 4, 6 and 8, Examiner's Answer.

have been stimulated with J3 amyloid, that C1 promotes cell death in SK-N-AS cells (*human* neuroblastoma cells) and that C1 inhibits secretion of A1340 and A1342 in IMR-32 cells (*human* neuroblastoma cells). Thus, at least four functions and biological significances of C1 are set forth in Appellants' specification.

Regarding the state of the art in the relevant time frame, a connection between Alzheimer's disease and Aβ was clear. *See* Seubert *et al.*,[3] made of record by Appellants on October 28, 2008. Appellants' experimental results showing decreased secretion of Aβ from cells transfected with C1 proves the specific, substantial and credible utility of the claimed protein to diagnose and treat Alzheimer's disease because of the known role of neurodegenerative disease and Aβ, for example. Further, Siemers et al. and Fleisher et al.[4] report the use of the compound LY450139 (an inhibitor of γ-secretase, the enzyme that is involved in producing Aβ peptide from APP), having Aβ secretion inhibitory activity, as a *therapeutic* agent for Alzheimer's disease in clinical trials. *See* Siemers et al. and Fleisher et al., made of record by Appellants on October 28, 2008. Thus, the evidence of record provides detailed information about the claimed subject matter, such as full and novel C1 polypeptides, full and novel DNAs, expression analysis under highly regulated experimental conditions, differential expression in specific tissues and cells, differential expression in specific tissues and cells under specific

[3] Peter SEUBERT et al., "Isolation and quantification of soluble Alzheimer's β-peptide from biological fluids", Nature, 1992, 359: 325-327.

[4] Adam S. FLEISHER, MD. et al., "Phase 2 Safety Trial Targeting Amyloid β Production with a γ-Secretase Inhibitor in Alzheimer Disease", Arch Neurol, 2008, 65(8): 1031-1038.

cellular conditions, highly specific relations between cell state and C1, inhibitory activity by C1 against Aβ secretion and the significance of Aβ in neurodegenerative disease. A person of ordinary skill in the art would immediately appreciate that Appellants' invention is useful based on the evidence of record.

B. The Record Shows That The Claimed Proteins And Encoding Nucleic Acids Have A Role in Neurodegenerative Disease

The Office asserts that the record (including Appellants' specification, working examples, state of the art references and Declaration evidence) fails to include any credible evidence proving a role for Appellants' C1 protein in nuerodegenerative disease. See, *inter alia*, pages 5, 9, 10, 12, 13, and 16, Examiner's Answer.[5]

Appellants respectfully disagree. Initially, 35 U.S.C. § 101 does not require that a claimed biomolecule have a role in disease in order to have a utility.

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[5] Specifically, according to the Office, "the specification does not disclose any scientific reasoning as how these data explain the role of C1 protein in Alzheimer's disease, Down's syndrome, prion disease or any other neurodegenerative diseases"; "the results of Example 4 do not allow a conclusion that C1 is useful to prevent or treat AD"; "the record shows that it is not the administration of C1 but the artificial overexpression of the C1 gene causes changes in secretion of amyloid"; "the Declaration is insufficient…because it is limited to presenting additional data obtained on cells transfected with C1 protein and studied for cell death promotion activity and secretion of αβ"; "Seubert et al. does not teach that any protein that is artificially introduced into a transfected cell line changes spontaneous αβ release becomes immediately suitable as a useful therapeutic compound to prevent or treat Alzheimer's disease"; "there is no record of suppression of αβ secretion upon administration of C1"; "provided that significance of the 'endoplasmic reticulum stress' is not fully explained in the etiology of neurodegeneration and that cells artificially transfected with a novel nucleic acid are not an art-recognized model for Alheimer's disease pathology, the specification provides no meaningful explanation regarding relationship between C1 and αβ secretion processes…". See, *inter alia*, pages 10, 11, 12 and 16, Examiner's Answer.

At page 12 of the Examiner's Answer, the Examiner admits, "the results of scientific experiments presented in the specification as filed are not doubted or disputed by the Examiner." However, the Examiner is incorrect that "the specification does not disclose any scientific reasoning as how these data explain the role of C1 protein in Alzheimer's disease, Down's syndrome, prion disease or any other neurodegenerative diseases." Pages 2 and 70 of Appellants' specification states, "in recent years, the relationship between various neurodegenerative diseases and endoplasmic reticulum stress has been regarded important" and "it is also reported that a cell having an abnormality in prelininin 1 as a causative gene of familial Alzheimer's disease is made vulnerable to endoplasmic reticulum stress, and production of β-amyloid is increased due to lack of IreI participating in endoplasmic reticulum stress response...". Pages 1-2, specification. This means that the nexus between ER stress, Aβ (including enhanced production of β-amyloid) and neurodegenerative disease was and is appreciated. Furthermore, page 2 of the specification indicates, "the present inventors estimated that a target gene for creating a medicine for neurodegenerative diseases can be found in genes participating in endoplasmic reticulum stress response, and they made an exhaustive analysis of gene expression in nerve cells against endoplasmic reticulum stress, and as a result of extensive study, they found a novel gene whose expression was significantly increased upon application of endoplasmic reticulum stress to nerve cells." [Emphasis added].

Regarding Appellants' scientific evidence, the Examiner's assertions that "the results of Example 4 do not allow a conclusion that C1 is useful to prevent or treat AD"; "the record shows that it is not the administration of C1 but the artificial overexpression of the C1 gene causes

changes in secretion of amyloid"; and "the Declaration is insufficient...because it is limited to presenting additional data obtained on cells transfected with C1 protein and studied for cell death promotion activity and secretion of αβ" is scientifically unsupported and mere conjecture. Section 706.03 of the MPEP explicitly cautions the Office that "[w]here a major technical rejection is proper (e.g., lack of proper disclosure, undue breadth, utility, etc.) such rejection should be stated with a full development of the reasons rather than by a mere conclusion coupled with some stereotyped expression." The Examiner's mere conclusory statements fail to rebut Appellants' evidence of C1's role in neurodegenerative diseases vis-à-vis endoplasmic reticulum stress responses in nerve cells - an undisputable utility. Regarding Office personnel making scientific assertions in conducting a utility analysis, the MPEP clearly states:

> "...where an applicant has set forth a specific and substantial utility, courts have been reluctant to uphold a rejection under 35 U.S.C. 101 solely on the basis that the applicant's opinion as to the nature of the specific and substantial utility was inaccurate....Practical considerations require the Office to rely on the inventor's understanding of his or her invention in determining whether and in what regard an invention is believed to be "useful." Because of this, Office personnel should focus on and be receptive to assertions made by the applicant that an invention is "useful" for a particular reason." MPEP § 2107.01.

But the Office does just the opposite, offering no more than speculative critical interpretations of Appellants' evidence.[6] Appellants' evidence (including Appellants' specification, working

[6] See, page 11, Examiner's Answer, wherein the Examiner asserts, "the record shows that it is not the administration of C1 but the artificial overexpression of the C1 gene [that] causes changes in secretion of amyloid". Appellants' Appeal Brief points out that the court in *Brana* held that human testing is not required - "the stage at which an invention in this field becomes useful is **well before it is ready to be administered to human**". [Emphasis added] Appeal Brief, *inter alia*, pages 17-18. Thus, the ...(footnote continued)

examples, state of the art references and Declaration evidence, as more elaborately discussed in Appellants' Appeal Brief and highlighted herein in response to the allegations set forth in the Examiner's Answer) are summarily dismissed, which is improper.

Based upon the law[7], and for at least the foregoing reasons, there is sufficient evidence of record that the claimed proteins have a well-established or specific, substantial, and credible utility for, *inter alia*, C1.

C. Claims 1, 2, 4-7 and 17 are Patentable Under 35 U.S.C. § 112, First and Second Paragraph

At pages 7 to 8 of the Examiner's Answer, the Office rejects claims 1, 2, 4-7 and 17 under 35 U.S.C. § 112, first paragraph. Specifically, the Examiner admits that the rejection under 35 U.S.C. § 112, first paragraph is contingent on the rejection under 35 U.S.C. § 101, addressed above. Thus, for the reasons discussed above, in Section III Parts A and B, the Examiner erred in making the rejection and the rejection should be withdrawn.

At pages 7 to 8 of the Examiner's Answer, the Office maintains the rejection of claim 17 under 35 U.S.C. § 112, second paragraph. The Office's rejection is premised on the allegation that the C1 protein is not sufficiently characterized, which according to the Examiner is

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Examiner's conjecture that the experimental evidence provided is insufficient due to an absence of human administration and/or some other undisclosed bystandered effect is factually and legally incorrect.

[7] Appellants herein incorporate and apply all discussions of the law found, *inter alia*, in Appellants' Appeal Brief.

contingent on the rejection under 35 U.S.C. § 101. Thus, for the reasons discussed above, in Section III Parts A and B, the rejection should be withdrawn.

Respectfully submitted,

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Date: November 25, 2009